FINAL

121st MEETING OF THE NATIONAL CANCER ADVISORY BOARD (NCAB)
MEETING OF THE SUBCOMMITTEE ON CLINICAL INVESTIGATIONS

February 20, 2002
12:55 p.m. - 1:55 p.m.

Welcome/Opening Comments—Dr. Larry Norton

Dr. Larry Norton chaired the meeting of the Subcommittee on Clinical Investigations with Dr. Ellen Feigal, Acting Director, Division of Cancer Treatment and Diagnosis, serving as Executive Secretary. The two agenda items were: 1) Cancer Therapy Evaluation Program Pilot Projects; and 2) Implementation of NIH Policies on Data and Safety Monitoring of Clinical Trials. Dr. Norton directed attendees' attention to three handouts as background material for the discussion.

Cancer Therapy Evaluation Program Pilot Projects—Dr. Jeffrey Abrams

Dr. Abrams began his presentation by showing the home page of the Cancer Clinical Trials Web site. This Web site describes many of the changes taking place in clinical trials at the NCI in several broad areas, including: generating new research ideas; broadening access to clinical trials for both physicians and patients; developing education and communication initiatives related to clinical trials; and implementing new procedures for streamlining various aspects of clinical trials. Dr. Abrams then briefly described some of the changes taking place in the areas of generating new research ideas and streamlining procedures.

Generating New Research Ideas. Several new initiatives have been aimed at generating new research ideas. After describing the Implementation Committee Framework for Clinical Trials, Dr. Abrams focused on the State of the Science (SOTS) Meetings and the Concept Evaluation Panels (CEP). State of the Science Meetings have been held for lung cancers, genitourinary cancers, gastrointestinal cancers, and leukemia. Meetings planned for this year include those on leukemia, sarcoma, and pancreatic cancer. Important outcomes have resulted from each of these meetings and some examples of these outcomes were presented. Dr. Abrams noted that the SOTS are attended by only about 100 individuals to keep the meetings manageable; however, the meetings are accessible via the Internet to many. Web site usage of the SOTS meetings page has been monitored and is increasing. Additional evaluation of the SOTS is underway by measuring outcomes, performing meeting surveys, and developing of an OMB-approved survey of Web site users that will compare the multi-media presentation of the meetings to the standard text meeting summary.

Concept Evaluation Panels are broad-based, rigorous reviews of large, Phase III trials. CEPs have been convened for genitourinary and lung cancers. The Genitourinary CEP has reviewed 19 concepts and the Lung CEP has reviewed 21 concepts. Of the 40 combined concepts, 15 have been approved, 11 recommended for revision and resubmission, and 14 have been disapproved. These numbers represent an increase from those seen prior to the implementation of the CEPs. Evaluation of the CEPs has shown that the Panel members generally support the process of CEP review and agree that the 'bar' has been set higher for trials. Panel members wanted to see increased communication between the CEPs and the investigators and wanted to have face-to-

face meetings periodically. The scoring system was deemed too complex and so a simplified model was adopted.

Streamlining Procedures. Several initiatives are underway to streamline procedures related to clinical trials. These include the formation of the Clinical Trials Support Unit (CTSU), new informed consent procedures, a centralized Institutional Review Board (CIRB), new protocol assembly, and the Clinical Trials Monitoring Branch Audit Information System (CTMBAIS). Dr. Abrams focused his presentation on the CTSU and the CIRB.

The CTSU has two major goals: 1) to improve efficiency for all Cooperative Group studies; and 2) to provide access to many NCI-sponsored Phase III studies for Cooperative Group members and other investigators. Dr. Abrams explained the benefits of the CTSU in terms of improving efficiency for the investigators. Investigators can register once for all Groups. There is also coordination of all on-site auditing of the Group participants. Beginning in 2002, the CTSU will fully deploy its regulatory support system. Through the use of clinical data transfer, they are also working on the elimination of the need to transfer paper case report forms (CRFs). Common data element implementation has begun and is in place for several cancer types. By the end of the year, common data elements should be in place for every cancer type covered by the Cooperative Groups. The CTSU is also working on remote data capture, which will be a Web-based system that will allow on-line collection of data, enabling real-time data checking and reducing data queries. These streamlining processes are collaborative efforts involving the CTSU, CTEP, and Cooperative Groups trying to mesh disparate data collections systems. With respect to access, Dr. Abrams described the increases in accrual by the CTSU over the past year and a quarter. He stated that the CTSU wants to improve the menu of trials available and described several ways they planned on increasing accrual. They are going to endorse specific studies, allow intergroup participation via CTSU, open the CTSU to all qualified US oncologists beginning in May 2002, and fully implement the Central IRB.

Dr. Abrams then described the status of the Central IRB. The pilot program of the CIRB was begun in August of 1999. In May of 2000 they met with 25 local IRB representatives. He described the procedure the CIRB follows for approving protocols. The CIRB Pilot has been meeting monthly and they plan to expand to include more local IRB sites in the near future. The program remains an active collaboration between Office of Human Research Protection (OHRP) and NCI. Dr. Abrams described the plans that are underway to evaluate the CIRB. The evaluation will include 'satisfaction' surveys of involved parties and quantitative measures of administrative performance. These will be performed by outside contractors.

During the discussion of this topic, it was suggested that the CTSU try to attract surgeons in addition to medical or radiation oncologists. The question was asked if there was any evidence that more investigators are being brought into the system to solve the access problem.

The response was that it is too early to tell. When the system is opened up to all qualified oncologists and related disciplines, they will be better able to answer that question. Dr. Christian noted that in a separate pilot entitled the Expanded Participation Pilot, some of the smaller practices are accruing at 50% or greater of the rate for Cooperative Group members.

It was noted that there needs to be more 'buy in' by the large institutions to the idea of the CIRB, and there may be a reluctance of local IRBs to relinquish authority. Dr. Norton suggested that this issue be brought back to the Subcommittee (and possibly to the NCAB) in the future to look at the issue of a centralized bureaucracy slowing down the approval process because of duplication of the review process and what effect that might have. Dr. Christian noted that while the approval process may slow with a CIRB, the accrual rate should increase dramatically if the decision of CIRB expedites or perhaps substitutes for the approval process of the local IRB.

Implementation of NIH Policies on Data and Safety Monitoring of Clinical Trials —Dr. Margaret E. Holmes

Dr. Holmes briefly described the background of the Data and Safety Monitoring of Clinical Trials. She stated that the NIH had published policies related to data and safety monitoring in 1998 and 1999 and that compliance began in October 2001. NCI sent letters to grantees informing them of the new policies. NCI then formed a review panel to look at the data and safety monitoring (DSM) plans from NCI-designated Cancer Centers. They looked at the procedures and review criteria and essential elements of the DSM plans. At about this same time, NCI published its "Essential Elements of a Data and Safety Monitoring Plan for Clinical Trials Funded by the National Cancer Institute." Dr. Holmes described the essential elements of a DSM plan, which were written for individual investigators and also for institutions. DSM plans should tailor their monitoring activities to the degree of risk to participants and to the size and complexity of the trial. Other aspects that the report covered include: committees and individuals responsible for DSM, processes and policies for DSM, reporting of adverse events, temporary or permanent suspension of trials report to the NCI Program Director, and assuring data accuracy and protocol compliance and quality control for adverse event reporting.

Dr. Holmes explained that 52 of the 60 NCI-designated Cancer Centers conduct clinical trials. Of these, they have received and reviewed DSM plans for 47 institutions, approving 17 plans. The remainder have been either disapproved or conditionally approved. No penalties currently exist for those Centers without an approved plan. Dr. Holmes then showed a list of Cancer Centers which have received approval.

Plans exist for ongoing reviews of these DSMs. Changes and improvements of plans can be submitted in noncompeting continuing applications.

Discussion

The discussion centered around assessing the performance of the DSMs. Currently, there is no mechanism for doing this but it was acknowledged that such a process would be benficial. It was noted that the first step in this process was to give the community a means to operationalize the NIH policy. In the future, they may look to methods for assessing performance.

Larry Norton, M.D.
Chairman

Ellen Feigal, M.D.
Executive Secretary